REMARKS

Claims 1-26 are pending in the above-identified application, from which claims 2-4, 10-14, 17, 19, 22 and 24-26 are withdrawn from consideration. Claims 1, 5-9, 15, 16, 18, 20, 21 and 23 are rejected as discussed below. Claim 1 is amended to recite a composition comprising a nucleic acid construct comprising: a transgene flanked by two terminal repeat sequences, wherein the terminal repeat sequences are derived from piggyBac transposon; and a nucleic acid sequence encoding a chimeric integrating enzyme under the control of a promoter element, the chimeric integrating enzyme comprising a DNA binding domain and an enzymatic integrating domain, wherein the DNA binding domain is derived from a zinc finger domain and wherein the enzymatic integrating domain is derived from piggyBac transposase. Support for the amendment can be found, for example, page 9, lines 21-33 (paragraph 52); page 11, lines 13-16 (paragraph 59); page 14, lines 1-22 (paragraphs 72-74); page 16, lines 5-13 (within paragraph 82); page 29, lines 15-16 (paragraph 121); and Example 18 of the specification as filed as well as in the claims as originally filed. Claims 15, 18-20 and 24 are amended to provide proper antecedent basis in the dependent claims, including amending the dependencies of claims 18, 19 and 24. Claims 7-14, 16, 17, 21 and 22 are cancelled without prejudice. The specification is amended to replace the sequence listing with the substitute sequence listing filed herewith. In addition, the specification is amended to include corresponding sequence identifiers (SEQ ID NOs: 13 and 14) in the Brief Description of Drawings section. No new matter is added by way of these amendments. Upon entry of the response, Claims 1-6, 15, 18-20 and 23-26 will be pending, Claims 2-4, 19, 25 and 26 remain withdrawn, and Claims 1, 5, 6, 15, 18, 20, 23 and 24 are presented for further examination.

Presentation of Claim 24 for further examination

In the Office Action, Claim 24 was withdrawn from further consideration as being drawn to a non-elected invention. Claim 24 is currently amended to depend from Claim 23 to provide proper antecedent basis. As Claim 23 is currently under examination in the application, Applicant respectfully submits amended Claim 24 for further examination.

Objection to the Specification

The disclosure is objected to for failing to comply with the requirements of 37 C.F.R. §§1.821-1.825 because sequences set forth in the specification, specifically in Figure 16 and at page 76, Table 3, lack sequence identifiers.

In response, Applicant respectfully submits a substitute sequence listing in paper and computer readable format and a substitute sequence submission statement. In addition, the specification is amended to replace the sequence listing with the substitute sequence listing filed herewith and to amend the Brief Description of Drawings to include corresponding sequence identifiers (SEQ ID NOs: 13 and 14) in the section. No new matter is added by way of this amendment.

Substitute Sequence Submission Statement

The substitute sequence listing is provided to include sequences disclosed in Figure 16 and at page 76, Table 3 of the specification as filed. No new matter is added by this amendment.

A copy of the substitute sequence listing in computer readable form as required by 37 C.F.R. §1.821(e) is submitted herewith in electronic format. The electronic format of the Substitute Sequence Listing is provided as a file entitled 002-081002-SUB_SEQ_LIST-40000212-0027.TXT, created October 2, 2008, which is 3 Kb in size.

As required by 37 C.F.R. §1.821(f), I hereby declare that the information uploaded as electronic file 002-081002-SUB_SEQ_LIST-40000212-0027.TXT, created October 2, 2008, which is 3 Kb in size, is identical to the substitute sequence listing filed herewith. Accordingly, no new matter has been introduced.

Rejection of Claims Under 35 U.S.C. §103

Claims 1, 5-9, 15-16, 18 and 20 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Handler *et al.* (1998. *PNAS* 95:7520-7525, hereinafter referred to as "Handler") in view of Kim *et al.* (U.S. Patent No. 6,479,626, hereinafter referred to as "the '626 patent"), Katz *et al.* (1996. *Virology* 217:178-190, hereinafter referred to as "Katz") and Elledge *et al.* (U.S. Patent No. 6,828,093, hereinafter referred to as "the '093 patent"). Claims 20-21 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the same combination, as

applied to claims 1, 5-9, 15-16, 18 and 20, and further in view of Grigliatti *et al.* (U.S. Patent Publication No. 2002/0116723, hereinafter referred to as "the '723 publication"). In addition, Claim 23 is rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the same combination, as applied to claims 1, 5-9, 15-16, 18 and 20-21, and further in view of McFarlane *et al.* (1996. *Transgenic Res.* 5(3):171-177; Abstract only, hereinafter referred to as "McFarlane"). Applicants respectfully disagree, as discussed below.

Standard for Obviousness

The Patent and Trademark Office has the burden under section 103 to establish a *prima facie* case of obviousness. *In re Piasecki*, 745 F.2d 1468, 1471-72, 223 USPQ 785, 787-87 (Fed. Cir. 1984). An essential characteristic of any *prima facie* case of obviousness is that the references, when combined, must teach or suggest all the claim limitations. The present rejection fails to make a *prima facie* case of obviousness because the references in combination fail to supply at least one element common to all of the claims in consideration.

The Claims

The claims relate to a composition containing a single nucleic acid construct that includes (i) a transgene, flanked by piggyBac transposon-derived terminal repeats, to be integrated into a target host genome for non-transient expression in the host, and (ii) a nucleic acid sequence that encodes a chimeric integrating enzyme that catalyzes integration of the transgene into the target host genome. The chimeric integrating enzyme includes a zinc-finger-derived DNA binding domain as well as an enzymatic integrating domain derived from piggyBac transposase. Accordingly, Claim 1 recites a composition comprising a nucleic acid construct comprising: a transgene flanked by two terminal repeat sequences, wherein the terminal repeat sequences are derived from piggyBac transposon; and a nucleic acid sequence encoding a chimeric integrating enzyme under the control of a promoter element, comprising a DNA binding domain and an enzymatic integrating domain, wherein the DNA binding domain is derived from a zinc finger domain and wherein the enzymatic integrating domain is derived from piggyBac transposase. Claims 5-6, 15, 18, 20, 23 and 24 depend from Claim 1 and contain all the features thereof as well as additional features recited in the claims. Claims 7-14, 16, 17, 21 and 22 are cancelled without prejudice.

No Prima Facie Case Has Been Established

Claims 1, 5-9, 15-16, 18 and 20 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Handler in view of the '626 patent, Katz, and the '093 patent. However, the combination of references does not teach or suggest all the claim limitations.

Handler teaches germ-line transformation of a medfly *we* host strain using two separate vectors, a first vector encoding a transgene (the medfly *w* gene) and a second vector encoding the normally regulated piggyBac transposase. However, Handler does not teach or suggest the claimed composition; specifically, Handler does not teach or suggest **a single nucleic acid construct** comprising a transgene and a nucleic acid encoding a chimeric integrating enzyme, the chimeric integrating enzyme comprising an enzymatic integrating domain derived from piggyBac transposase, as claimed.

The '626 patent is relied upon for teaching that DNA binding domains include zinc finger proteins and helix-loop-helix motifs. However, the reference is directed only to providing design strategies for flexible linkers that fuse two DNA binding domains of a "chimeric zinc finger protein." The "chimeric zinc finger protein" is composed of two or more DNA-binding domains, one of which is a zinc finger polypeptide, wherein the two domains can be the same or heterologous. The '626 patent is silent with respect to recited features of the claimed composition, which comprises **a single nucleic acid construct** comprising a transgene and a nucleic acid encoding a **chimeric integrating enzyme**, wherein the chimeric integrating enzyme comprises an enzymatic integrating domain derived from piggyBac transposase. Thus, the '626 patent does not repair the deficiencies of Handler.

Katz is relied upon for teaching a chimeric integrating enzyme that contains the DNA-binding domain of LexA repressor protein fused to the catalytic domain of integrase enzyme. However, Katz is also silent with respect to recited features of the claimed composition, which relates to **a single nucleic acid construct** comprising a transgene and a nucleic acid encoding a chimeric integrating enzyme, wherein the chimeric integrating enzyme comprises DNA binding domain derived from a zinc finger domain and an enzymatic integrating domain derived from **piggyBac transposase**. Accordingly, Katz does not repair the deficiencies of Handler.

The '093 patent is relied upon for deducing, at the time of the invention, that piggyBac transposase was an art-recognized species within the genus of site-specific recombination enzymes comprising transposases, integrases and recombinases. However, the '093 patent does not provide any relevant disclosure to the claimed composition and does not teach or suggest recited features of the claims, which relate to **a single nucleic acid construct** comprising a transgene and a nucleic acid encoding a chimeric integrating enzyme, wherein the chimeric integrating enzyme comprises DNA binding domain derived from a zinc finger domain and an enzymatic integrating domain derived from piggyBac transposase. Thus, the '093 patent does not repair the deficiencies of Handler.

Accordingly, Handler alone or in combination with the '626 patent, Katz and the '093 patent does not teach all the features of the claims and therefore does not set forth a *prima facie* case of obviousness. In view of the foregoing, Applicant respectfully submits that Claim 1 and dependent Claims 5-6, 15, 18, 20, 23 and 24 are patentable over the cited references in combination or alone. Withdrawal of the rejection of claims under 35 U.S.C. §103 is respectfully requested.

The disclosure of the '723 publication

Claims 20-21 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Handler in view of the '626 patent, Katz, and the '093 patent, as applied to claims 1, 5-9, 15-16, 18 and 20, and further in view of Grigliatti *et al.* (U.S. Patent Publication No. 2002/0116723, hereinafter "the '723 publication"). The '723 publication is relied upon for teaching transposon-based transformation vectors comprising the use of piggyBac transposase. However, the '723 publication merely discloses vectors that include a transposon-based protein expression cassette comprising transposable elements defining a transposon and having a selectable marker gene and/or heterologous protein coding sequences within the transposon; such vectors may be introduced into cell lines having a source of transposase. The reference teaches that inducible transposase producing cell lines can be created for a wide spectrum of transposases, including piggyBac. In contrast, the claimed composition is directed to **a single nucleic acid construct** comprising a transgene and a nucleic acid encoding a chimeric integrating enzyme, wherein the chimeric integrating enzyme comprises an enzymatic integrating domain derived from piggyBac transposase. Thus, the recited construct includes a nucleic acid sequence that expresses a

catalytic integrating component rather than being dependent on host cell enzymes to carry out integration of the transgene. In view of the foregoing, the '723 does not repair the deficiencies of Handler, and the cited combination of references does not teach or suggest all the elements of the claims. Accordingly, Claims 20-21 are patentable over the cited combination of references, and withdrawal of the rejection under 35 U.S.C. §103 is respectfully requested.

The disclosure of McFarlane

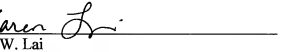
Claim 23 is rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Handler in view of the '626 patent, Katz, and the '093 patent, as applied to claims 1, 5-9, 15-16, 18 and 20-21, and further in view of McFarlane *et al.* (1996. *Transgenic Res.* 5(3):171-177; Abstract only, hereinafter referred to as "McFarlane"). McFarlane is relied upon for teaching the inclusion of a nucleic acid sequence having 5 base pairs that were homologous to the host DNA. However, McFarlane is silent with respect to recited features of the claimed composition, which relates to a single nucleic acid construct comprising a transgene flanked by terminal repeat sequences derived from piggyBac transposon and a nucleic acid encoding a chimeric integrating enzyme, wherein the chimeric integrating enzyme comprises an enzymatic integrating domain derived from piggyBac transposase. Accordingly, the reference does not repair the deficiencies of Handler, and the cited combination of references does not teach or suggest all the elements of the claims. Thus, Applicants respectfully submit that Claim 23 is patentable over the cited combination of references, and withdrawal of the rejection under 35 U.S.C. §103 is requested.

Conclusion

Applicant submits that the present Application is in condition for allowance and respectfully request the same. If any issues remain, the Examiner is cordially invited to contact Applicant's representative at the number provided below in order to resolve such issues promptly.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 19-3140.

Respectfully submitted,

Dated: October 10, 2008 By: 

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